

## **REMARKS**

Applicants request entry of the Substitute Sequence Listing submitted herewith. The Sequence Listing has been amended to include SEQ ID NO:89 corresponding to the cDNA sequence spanning the junction between exons 19 and 21 of IKAP when exons 19 and 21 are directly joined. There is support in the specification for such a sequence. In fact, there is support for such a sequence in the priority application, U.S. provisional patent application 60/260,080 filed January 6, 2001 (hereafter “the ‘080 application”), as well.

Support for the sequence can be found on page 6, lines 1-5, page 13, lines 3-16, and Figure 2C of the ‘080 application. Although the borders of exon 20 are not explicitly recited in the ‘080 application, it can be deduced using only the disclosed information. First, exon 20 is shown to be 74 nucleotides by Figure 5. RT-PCR on neuronal tissue from an FD patient using primers 19F and 23F yielded a 319 bp band. Wild type cDNA yields a 393 bp band when the same primers are used for RT-PCR. Because the ‘080 application discloses that the consequence of an FD1 mutation is the skipping of exon 20 (see page 6, lines 3-5 of the ‘080 application), one skilled in the art would realize that exon 20 is 74 bp (393-319). Secondly, the ‘080 application discloses that the FD1 mutation is a T to C change at residue 6 of intron 20 (see page 2, lines 27-28 of the ‘080 application). Figure 1 shows that intron 20 is 3’ to exon 20. Thus exon 20 ends 6 residues previous to the FD1 mutation. Once exon 20 is identified on the IKAP genomic sequence given in Figure 6, the corresponding sequence could be identified on the IKAP cDNA. Using this information, one skilled in the art could identify that exon 20 is between 2,441 and 2,514 of the IKAP cDNA. Additionally, the nucleic acid sequence of the exon 19/21 junction is evident in Figure 2C by reading the sequencing gel shown for the IKAP cDNA of an FD patient.

Accordingly, because the precise exon 19/21 border is shown, the nucleotides that span the junction (*i.e.*, SEQ ID NO:89) are easily deduced.

Thus, no new matter is included in the Substitute Sequence Listing.

### **CONCLUSION**

Applicants respectfully request that the Substitute Sequence Listing be entered.

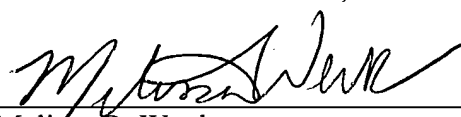
### **AUTHORIZATION**

No fee is believed to be due in addition to the Extension of Time submitted herewith. However, the Commissioner is hereby authorized to charge any additional fees which may be required for consideration of this Amendment to Deposit Account No. 13-4500, Order No. 1829-4004US1.

Respectfully submitted,  
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By: \_\_\_\_\_

  
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